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Research Article

Comparison between Platelet Rich Plasma and 5. FU on Post Burn Leukoderma.

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Abstract

Background: Post-burn leucoderma, characterized by persistent hypopigmentation, presents significant therapeutic challenges due to the disruption of melanocyte function and melanin production. Platelet-Rich Plasma (PRP) and 5-Fluorouracil (5-FU) have emerged as promising interventions, but their comparative efficacy remains underexplored. **Objective:** This study aimed to evaluate the comparative effectiveness of PRP and 5-FU in repigmentation and scar remodeling in patients with post-burn leucoderma. **Methods:** A comparative clinical study was conducted on 20 patients with post-burn leucoderma using a split-lesion design. PRP was prepared through a two-step centrifugation process and applied after microneedling. A 5% 5-FU solution was injected intradermally at specific intervals. Outcomes were assessed through clinical, photographic, and histopathological evaluations over six months. **Results:** PRP and 5-FU therapies demonstrated progressive pigmentation improvement, with 55% of participants achieving dark pigmentation by six months. Lesion site and size significantly influenced outcomes, with upper limb lesions responding better than lower limb and trunk lesions. A significant inverse relationship was observed between 5-FU injection volumes and pigmentation improvement. Histopathological analysis showed partial restoration of melanocytes and reduced dermal inflammation. **Conclusion:** Both PRP and 5-FU are effective in managing post-burn leucoderma, with PRP demonstrating consistent results and 5-FU requiring precise dosing to optimize outcomes. These findings emphasize the need for tailored therapeutic approaches to improve patient quality of life.

Keywords: 5-Fluorouracil (5-FU), Platelet-rich plasma (PRP), transforming growth factor (TGF)

Introduction

Skin pigmentation is a complex biological process involving the synthesis of melanin within melanosome vesicles, which reside in melanocytes located in the basal layer of the epidermis. These melanocytes transfer melanosomes to adjacent keratinocytes through dendritic-like processes, forming an epidermal-melanin unit that ensures pigmentation uniformity across the skin [1]. In post-burn leukoderma, this process is disrupted due to melanin loss at the basal layer, often compounded by fibrotic changes that inhibit melanocyte migration and melanin production in the affected area [2]. This hypopigmentation is not only disfiguring but also typically permanent, necessitating the development of effective therapeutic interventions.

Post-burn depigmentation is attributed to multiple undefined causes, but the destruction or loss of melanocytes in the basal layer and the formation of fibrotic scars are considered significant barriers to melanocyte migration and melanin transfer. Pathological examinations of depigmented post-burn skin have revealed reduced melanocyte numbers in the basal cell layer, emphasizing the need for

treatments aimed at increasing melanocyte density and removing scar tissue to restore pigmentation [3].

Treatment strategies for post-burn leukoderma often draw inspiration from therapies used for vitiligo. However, unlike vitiligo, where melanocytes are completely destroyed by immune mechanisms, melanocytes in post-burn leukoderma are present but have impaired melanin production. Research has shown that both hypopigmented and hyperpigmented post-burn scars contain similar numbers of melanocytes but differ in the quantity of melanin and α-melanocyte-stimulating hormone (α-MSH) [4].

Microneedling has emerged as a promising intervention for post-burn leukoderma due to its ability to stimulate the wound-healing cascade. This technique, which involves creating micro-injuries in the dermis with minimal epidermal damage, promotes collagen production and enhances skin rejuvenation, scar remodeling, and keratinocyte proliferation. Histological studies have demonstrated increased collagen types I, III, and VII and improved basal membrane integrity after microneedling, making it an effective tool for improving skin texture and pigmentation irregularities [5].

5-Fluorouracil (5-FU), an antimetabolite analogue of uracil, has shown potential in modulating pigmentation. While typically associated with hyperpigmented lesions during systemic cancer treatments, its topical application in wound environments inhibits epithelialization, delaying wound healing. Paradoxically, this delay may promote conditions conducive to melanocyte proliferation and subsequent pigmentation restoration in post-burn leucoderma [6].

Platelet-rich plasma (PRP) is another innovative approach gaining traction in dermatology. PRP consists of concentrated platelets, which release growth factors upon activation, including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor (TGF). These growth factors stimulate fibroblast proliferation, collagen synthesis, angiogenesis, and extracellular matrix remodeling, making PRP a promising candidate for treating conditions involving wound healing and skin regeneration [7].

This study aims to compare the efficacy of platelet-rich plasma and 5-fluorouracil in the treatment of post-burn leucoderma. By evaluating their effects on melanocyte proliferation, scar remodeling, and pigmentation restoration, this research seeks to establish an evidence-based approach for managing this challenging and often refractory condition.

Patients and Methods

Study Design

This was a comparative clinical study conducted at the Plastic Surgery Department, Minia University Hospitals, involving 20 patients diagnosed with post-burn leucoderma. The study utilized a split-lesion design to compare the efficacy of Platelet-Rich Plasma (PRP) and 5-Fluorouracil (5-FU) treatments.

Inclusion and Exclusion Criteria

Inclusion Criteria:

Patients with stable post-burn leucoderma of any burn type for a duration exceeding six months.

Exclusion Criteria:

Patients with hemorrhagic disorders, active infections at lesion sites, or compromised immune systems.

Study Procedures

Preoperative Preparation

Preoperative preparation involved obtaining comprehensive medical histories to identify factors affecting treatment outcomes, followed by a detailed clinical examination to evaluate lesion size, stability, and skin characteristics, along with an assessment of overall skin condition. Laboratory investigations, including CBC and RBS, were conducted to rule out contraindications. Standardized high-resolution photographs of lesions were taken at baseline and prior to each session to ensure consistent visual tracking of progress.

Intervention Techniques

Lesions were divided into two equal halves for intra-patient comparison. PRP was prepared

through a two-step centrifugation process using blood samples collected aseptically with acid citrate dextrose as an anticoagulant and applied after microneedling to enhance absorption and effectiveness. Microneedling involved using a dermaroller with 1.5 mm needles to create controlled micro-injuries in vertical, horizontal, and diagonal directions, stimulating skin regeneration. A 5% 5-FU solution was injected intradermally at 1 cm intervals using a fine insulin syringe, with the procedure repeated every two weeks for three sessions to promote melanocyte activation and repigmentation both sides of PRP and 5.FU injection sited can be spread by derma roller if the lesion on same site.

Postoperative Follow-Up

Postoperative follow-up included evaluations at three and six months post-intervention, with serial photographs taken during each visit to monitor treatment progress. Patients were educated on potential side effects and wound care, ensuring prompt management of any adverse events. Histopathological analysis through punch biopsies (3–4 mm) was conducted before treatment and three months afterward to assess changes in melanocyte density, inflammatory markers, and dermal alterations.

Outcome Measures

Outcome measures included systematic photographic comparisons to evaluate changes in pigmentation and scar texture, complemented by clinical assessments focusing on improvements in pigmentation, reduction of depigmented areas, and overall skin health. Histopathological analysis of pre- and post-treatment biopsies by punch biopsy from center of lesion was performed to identify cellular and structural changes, providing a comprehensive evaluation of treatment efficacy.

Statistical Analysis

Data were managed using Microsoft Excel and analyzed with IBM SPSS Statistics version 23.0. Descriptive statistics were used to summarize patient demographics and lesion characteristics. Comparative analyses included t-tests for quantitative variables, such as lesion size and pigmentation scores, and Chi-squared tests for categorical variables, such as treatment success rates. A significance level of $p < 0.05$ was established, with results falling below this threshold considered statistically significant.

Results

Patient Demographics

The study included 20 participants, equally distributed between males (n=10) and females (n=10) Non-randomized study. The mean age of males was 15.40 ± 6.10 years, ranging from 8 to 25 years, while the mean age of females was 17.60 ± 5.23 years, ranging from 10 to 23 years.

Table 1: Distribution of Age and Gender Among Participants

Gender	Number	Age (years) Mean ± SD	Minimum Age (years)	Maximum Age (years)
Male	10	15.40 ± 6.10	8	25
Female	10	17.60 ± 5.23	10	23

Burn Characteristics

Thermal burns were the most common (75%), followed by chemical burns (15%) and other types (10%). The mean lesion stability duration was 13.40 ± 4.63 months (range: 7–23 months), while the mean lesion size was 27.60 ± 14.87 cm² (range: 6–50 cm²).

The upper limb was the most affected site (50%), followed by the foot (20%) and lower limb (20%). The face and trunk were least affected (5% each). Normal skin was observed in 40% of cases, while hypopigmented and slightly fibrotic skin each accounted for 30%.

Table (2): Burn Characteristics

Burn Characteristics	Parameter	Number (%)
Burn Type	Thermal	15 (75%)
	Chemical	3 (15%)
	Other	2 (10%)
Lesion Site	Upper Limb	10 (50%)
	Foot	4 (20%)
	Lower Limb	4 (20%)
	Face	1 (5%)
	Trunk	1 (5%)
Lesion Characteristic	Normal	8 (60%)
	Hypopigmented	6 (30%)
	Slightly Fibrotic	6 (30%)

Comparison between pigmentation improvement groups by Lesion Site

Persistent erythema was the most common outcome at 1.5 months, with 90% of upper limb lesions showing this. Failed pigmentation was more common in lower limb and trunk lesions. At 3 months, 90% of lesions showed light pigmentation, while failed pigmentation persisted in foot, lower limb, and trunk lesions.

Table (3): Pigmentation Improvement by Lesion Site Over Time

Time	Pigmentation Improvement	Face	Foot	Lower Limb	Trunk	Upper Limb	P value
1.5M	**Failed Pigmentation**	0	1	3	1	1	0.073
	Persistent Erythema	1	3	1	0	9	
3M	**Failed Pigmentation**	0	3	3	1	1	0.040
	Light Pigmented	1	1	1	0	9	
6M	**Dark Pigmented**	1	1	1	0	8	0.113
	Failed Pigmentation	0	3	3	1	2	

Comparison between pigmentation improvement groups by 5-FU Injection Volume (mL)

The study found a correlation between 5-FU injection volume and pigmentation improvement. Patients with failed pigmentation received higher volumes at 1.5 months, while those with persistent erythema received lower volumes. Failed pigmentation was associated with higher volumes at 3 months, while light pigmentation had lower volumes.

Table (4): pigmentation improvement groups by 5-FU Injection Volume (mL)

Time	Pigmentation Improvement	5-FU Volume	P value
1.5M	**Failed Pigmentation**	4.41 ± 0.59	<0.001
	Persistent Erythema	2.05 ± 1.13	
3M	**Failed Pigmentation**	3.86 ± 1.15	0.003
	Light Pigmented	2.02 ± 1.23	
6M	**Dark Pigmented**	1.82 ± 1.04	<0.001
	Failed Pigmentation	3.91 ± 1.08	

Comparison between the outcome of Platelet Rich Plasma and 5-Fluorouracil

This table compares pigmentation improvement outcomes at three time points (1.5 months, 3 months, and 6 months) for Platelet-Rich Plasma (PRP) and 5-Fluorouracil treatment groups.

At 1.5 months, 5-Fluorouracil showed better outcomes for Persistent Erythema (64.29%) compared to PRP (35.71%), but PRP had a higher rate of Failed Pigmentation (66.67% vs. 33.33%). At 3 months, 5-Fluorouracil improved Light Pigmentation (58.33%), but PRP had a higher percentage of Failed Pigmentation (62.5%). At 6 months, 5-Fluorouracil outperformed PRP in Dark Pigmentation (72.73% vs. 27.27%), while PRP had a higher percentage of Failed Pigmentation (66.67%).

Table (5): pigmentation improvement groups between the outcome of PRP and 5-Fluorouracil

Time	Pigmentation Improvement	PRP N (%)	5-Fluorouracil N (%)	Total	P value
1.5M	**Failed Pigmentation**	4 (66.67%)	2 (33.33%)	6	0.02
	Persistent Erythema	5 (35.71%)	9 (64.29%)	14	0.01
3M	**Failed Pigmentation**	5 (62.5%)	3 (37.5%)	8	0.06
	Light Pigmented	5 (41.67%)	7 (58.33%)	12	0.03
6M	**Dark Pigmented**	3 (27.27%)	8 (72.73%)	11	0.01
	Failed Pigmentation	6 (66.67%)	3 (33.33%)	9	0.04

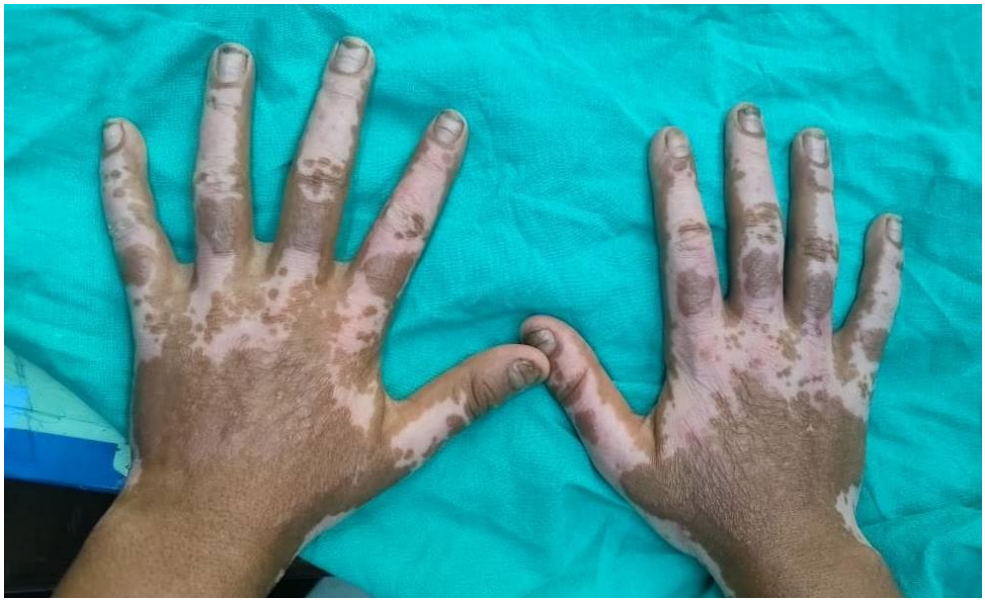

Figure (1): Preoperative Photograph Showing Post-Burn Leucoderma of both Hands.

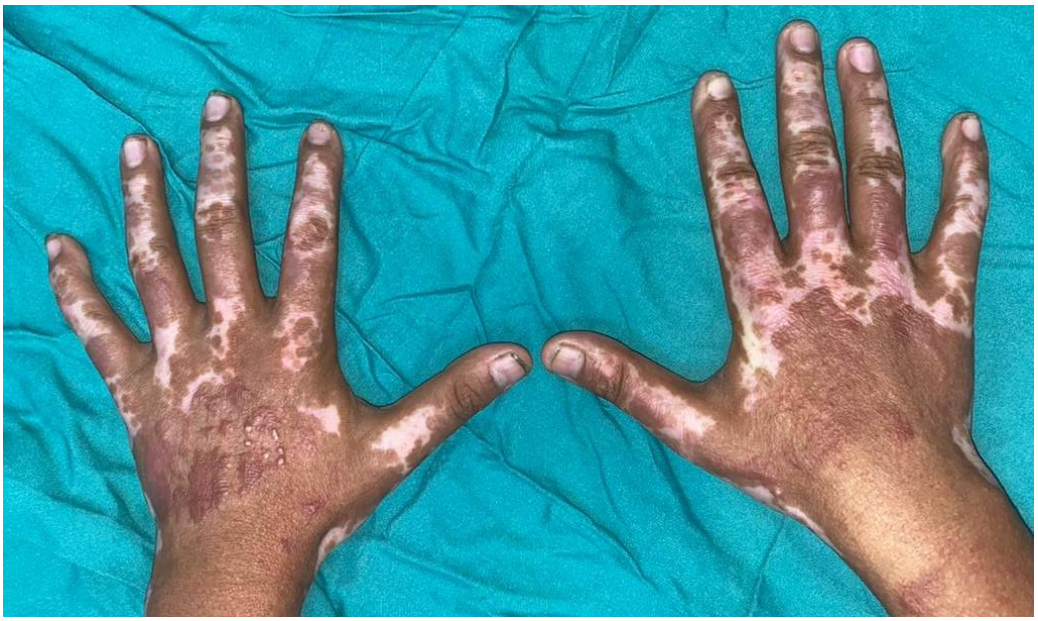

Figure (2): Three-Month Follow-Up Showing Significant Pigmentation Improvement in the 5-Fluorouracil Injection Area (left hand) (Dark and Light Pigmentation), and mild improvement in the PRP injection site (right hand).

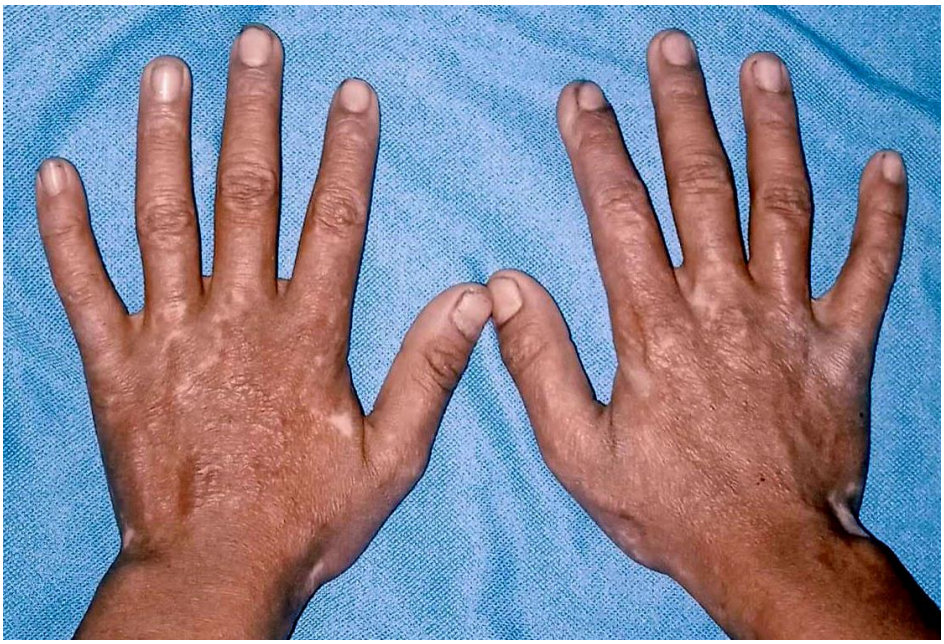

Figure (3): Six-Month Follow-Up Showing Significant Pigmentation Improvement in both hands.

Discussion

Post-burn leucoderma is a complex and challenging condition in reconstructive and aesthetic medicine, characterized by disfiguring hypopigmentation that significantly impacts patients' quality of life. This condition results from the loss or dysfunction of melanocytes in the basal epidermal layer, often compounded by scarring that impedes melanocyte migration and melanin production. Despite the availability of various therapeutic options, such as topical agents, surgical interventions, and laser therapies, achieving consistent and satisfactory repigmentation remains a major challenge. The need for effective, minimally invasive, and cost-

efficient treatment modalities has spurred research into alternative approaches.

This study evaluated the comparative efficacy of Platelet-Rich Plasma (PRP) and 5-Fluorouracil (5-FU) in promoting repigmentation in post-burn leucoderma. PRP is rich in growth factors, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and transforming growth factor-beta (TGF-β), which facilitate wound healing, angiogenesis, and collagen synthesis—processes critical for melanocyte activity and pigmentation restoration. Conversely, 5-FU, a chemotherapeutic agent, has demonstrated potential for stimulating melanocyte function through localized cytotoxic effects.

Our findings indicate that PRP and 5-FU therapies resulted in progressive pigmentation improvement over six months, with dark pigmentation achieved in 55% of participants. This outcome underscores the potential of these therapies in promoting melanocyte activity and repigmentation. These results align with El-Kamel and Alghobary (2014), who reported a 61.9% satisfaction rate with autologous punch minigrafting and topical khellin therapy under natural sunlight, suggesting that targeted interventions can yield comparable results [8].

Thermal burns were the most prevalent type, accounting for 75% of cases, consistent with global data from the WHO (2018) and Yakupu et al., (2022), which report that thermal burns, often caused by exposure to hot liquids, solids, or flames, are the most common type of burn injury globally[9]. Chemical burns, constituting 15% of cases, were more frequently observed in occupational settings due to exposure to industrial chemicals, reflecting a lower prevalence in the general population. The remaining 10% of cases included less common burn types, such as electrical and radiation burns, aligning with data from the American Burn Association (2023) [10].

The upper limbs were the most frequently affected sites, observed in 50% of cases, followed by the foot and lower limbs (20% each), with the face and trunk being the least affected (5% each). This distribution aligns with studies by Dissanaike and Rahimi (2009) and Ho and Ying (2001), who reported high incidences of upper limb burns due to protective reflexes. Such findings underscore the need for prevention strategies targeting vulnerable anatomical sites [11, 12].

Our study revealed a significant inverse relationship between lesion size and pigmentation improvement. Larger lesions were associated with failed pigmentation, while smaller lesions showed progressive stages of pigmentation improvement. These findings align with Hussein et al., (2023) and El-Kamel and Alghobary (2014), who noted better outcomes in smaller lesions due to reduced scar-induced impediments and easier melanocyte migration. Larger lesions pose challenges such as decreased vascular supply, disrupted extracellular matrix, and increased melanocyte depletion, highlighting the importance of early intervention [8, 13].

Lesion site also influenced pigmentation outcomes, with upper limb lesions showing faster and better repigmentation compared to other sites. At six months, dark pigmentation was achieved in 80% of upper limb lesions, whereas persistent depigmentation was more common in the foot, lower limbs, and trunk. Previous studies, including Hussein et al., (2023) and Elmohsen et al., (2014), reported similar findings, attributing improved outcomes in upper limb lesions to better vascularization and reduced mechanical stress, which facilitate melanocyte proliferation and migration [13, 14].

A significant inverse relationship was observed between the volume of 5-FU injections and pigmentation improvement. Higher volumes were associated with failed pigmentation, while lower volumes correlated with progressive improvement, ranging from persistent erythema to dark pigmentation. These findings suggest that higher 5-FU volumes may exert cytotoxic effects on melanocytes, hindering repigmentation. Similar dose-dependent effects were reported by Manuskiatti and Fitzpatrick (2002) in their study on intralesional 5-FU for keloids and hypertrophic scars [15].

In addition to injection volumes, the number of treatment sessions also influenced outcomes.

Participants with failed pigmentation completed more sessions, indicating a potential cumulative cytotoxic effect that adversely impacted melanocyte viability. Conversely, fewer sessions were associated with progressive pigmentation improvement. These findings emphasize the need for precise dosing and session optimization to balance therapeutic efficacy and minimize adverse effects.

Histopathological examination before treatment revealed structural abnormalities, including orthokeratosis, thickened basement membranes, and absent melanocytes in the basal layer. Post-treatment analysis demonstrated partial restoration of normal skin architecture, including melanocyte repopulation and reduced dermal inflammation. These findings are consistent with those of El-Kamel and Alghobary (2014), who noted similar structural improvements following targeted interventions [8].

The histopathological evidence supports the therapeutic potential of PRP and 5-FU in reversing pathological changes associated with post-burn leucoderma. Structural restoration is critical for melanocyte migration, survival, and melanin production, which are essential for effective repigmentation.

Our findings align with previous studies that explored various interventions for post-burn leucoderma. Hussein et al.. (2023) reported clinically significant repigmentation in 75% of cases treated with minced skin grafting, highlighting the efficacy of surgical precision in promoting pigmentation. Similarly, Elsayed et al., (2017) observed improvements in pigmentation scores with PRP, underscoring its role in promoting tissue repair and repigmentation [13, 16].

However, some studies, such as Ibrahim (2014), reported inconsistent outcomes with non-cultured epidermal transplantation, emphasizing the influence of patient demographics, lesion size, and anatomical location on treatment efficacy. These variations underscore the importance of tailoring therapeutic approaches to individual patient and lesion characteristics [14].

This study highlights the importance of optimizing 5-FU dosing strategies and integrating adjunctive therapies to improve clinical outcomes in post-burn leucoderma. Lower 5-FU volumes were associated with enhanced repigmentation, suggesting that precise dosing can minimize cytotoxic effects on melanocytes while maximizing therapeutic efficacy. Combining 5-FU with PRP or narrowband UVB phototherapy may further enhance outcomes by supporting melanocyte activity and improving skin architecture.

The association between lesion size and pigmentation outcomes underscores the need for early intervention, particularly for smaller lesions, to maximize treatment efficacy. Future studies should focus on long-term follow-up and comparative trials involving combination therapies to establish standardized protocols for this challenging condition.

Conclusion

The study demonstrates the effectiveness of Platelet-Rich Plasma (PRP) and 5-Fluorouracil (5-FU) in promoting repigmentation in post-burn leucoderma. PRP stimulates melanocyte activity and scar remodeling, while 5-FU improves pigmentation outcomes. The study emphasizes the need for individualized treatment protocols and adjunctive therapies.

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